

# Modulating the processing of emotional stimuli by cognitive demand

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**Emotional processing is influenced by cognitive processes and vice versa, indicating a profound interaction of these domains. The investigation of the neural mechanisms underlying this interaction is not only highly relevant for understanding the organization of human brain function. Rather, it may also help in understanding dysregulated emotions in affective disorders and in elucidating the neurobiology of cognitive behavioural therapy (e.g. in borderline personality disorder), which aims at modulating dysfunctional emotion processes by cognitive techniques, such as restructuring. In the majority of earlier studies investigating the interaction of emotions and cognition, the main focus has been on the investigation of the effects of emotional stimuli or, more general, emotional processing, e.g. instituted by emotional material that needed to be processed, on cognitive performance and neural activation patterns. Here we pursued the opposite approach and investigated the modulation of implicit processing of emotional stimuli by cognitive demands using an event-related functional magnetic resonance imaging—study on a motor short-term memory paradigm with emotional interferences. Subjects were visually presented a finger-sequence consisting either of four (easy condition) or six (difficult condition) items, which they had to memorize. After a short pause positive, negative or neutral International affective picture system pictures or a green dot (as control condition) were presented. Subjects were instructed to reproduce the memorized sequence manually as soon as the picture disappeared. Analysis showed that with increasing cognitive demand (long relative to short sequences), neural responses to emotional pictures were significantly reduced in amygdala and orbitofrontal cortex. In contrast, the more difficult task evoked stronger activation in a widespread frontoparietal network. As stimuli were task-relevant go-cues and hence had to be processed perceptually, we would interpret this as a specific attenuation of affective responses by concurrent cognitive processing—potentially reflecting a relocation of resources mediated by the frontoparietal network.**

**Keywords:** neuroimaging; distraction; cognition; attention; valence

## INTRODUCTION

It is widely acknowledged that emotional processing can be influenced by concurrent cognitive demand and *vice versa* (Pauly *et al.*, 2008). Several functional imaging studies have already investigated the interaction between affective and cognitive processes in the human brain (Gray *et al.*, 2002; Habel *et al.*, 2007). The majority focused mainly on the effects of emotional stimuli or, more general, emotion processing on cognitive performance and neuronal activation patterns.

Most of these studies suggested that affective factors and emotional states may (negatively) influence the performance in different cognitive tasks (Brown *et al.*, 1994). For example, emotional distracters may disrupt goal-directed processing

in healthy individuals (Vuilleumier *et al.*, 2001). Other studies, however, have indicated that emotional states can enhance or impair cognitive performance depending on the emotional valence and the cognitive process involved (Gray, 2001). Habel *et al.* (2007) examined the effects of negative and neutral olfactory stimulation on a simple attention (0-back) and a more demanding working-memory (2-back) task. A significant interaction between affect and cognitive demand has been shown, but also that individuals vary in their susceptibility to such emotional influences. Their data is hence in line with the hypothesis (Pessoa *et al.*, 2002a, 2005) that emotional stimuli interfere with cognitive processing especially when the task is demanding or resources are meagre.

In summary, results of studies investigating the impact of concurrent emotional stimuli or states on cognitive processes are inconsistent, which may at least in part relate to differences in experimental design (Sommer *et al.*, 2008). For example, different groups investigated the impact of induced emotional states on cognitive processes, employed emotional

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distracters or focussed on cognitive processing of emotional rather than neutral stimuli.

It has also been shown that concurrent cognitive engagement may be associated with a reduction of the activity in regions implicated with emotional responding, such as the amygdala and medial frontal cortex. Blair *et al.* (2005, 2007) showed significantly reduced amygdala activity in response to task-irrelevant negative emotional stimuli during the more cognitively demanding task trials and proposed a competition for attentional resources as the underlying mechanism of this effect. Consequently, less attentional resources should be devoted to the amygdala under concurrent cognitive demand. In line with this view, attention-demanding tasks have been found to attenuate the emotional impact of negative stimuli (Glynn *et al.*, 2002; Erthal *et al.*, 2005; Erk *et al.*, 2007). Finally, subjects even reported less negative feelings in response to negative pictures when they subsequently tried to solve complex rather than simple math equations (Van Dillen and Koole, 2007), demonstrating that cognitively demanding tasks may even down-regulate the emotional responses to previously displayed stimuli (Van Dillen *et al.*, 2009). Bishop *et al.* (2004) in contrast proposed that higher cognitive processing load is only associated with increased activity in areas sustaining these processes, while emotional processing in the amygdala, being a highly automated process, is hardly effected by other processes (cf. Behrmann *et al.*, 2004).

The aim of the present study is to investigate the interaction between cognitive load (operationalized by task difficulty) and processing of emotional stimuli in a situation where emotional stimuli are task-relevant and thus have to be explicitly attended to. That is, we addressed the question, whether emotional responses are also attenuated if they could not be ignored.

To this end, we assessed neuronal activity while healthy subjects performed a sequence reproduction task during which emotional stimuli from the International affective picture system (IAPS) served as the go-cues. The latter aspect ensured that subjects had to overtly attend to the emotional stimuli, which is not the case, e.g. in emotional distracter paradigms, without directly combining cognitive and emotional aspects, as it is the case in, e.g. emotional n-back paradigms. Furthermore, to differentiate the processing of emotional stimuli from the processing of complex stimuli *per se*, both, a low level (circle) and high level (neutral picture) control condition were implemented.

## MATERIALS AND METHODS

### Subjects

We examined 36 healthy volunteers (age-range 20–52 years, mean age 25.31 years; s.d.: 6.97; 17 females) without any record of neurological or psychiatric disorders and normal or corrected-to-normal vision. Absence of neuro-psychiatric disorders was confirmed using the structured interview StrukturiertesKlinisches Interview für DSM-IV (SKID)

(Wittchen *et al.*, 1997). All subjects gave informed written consent to the study protocol, which had been approved by the local ethics committee of the School of Medicine of the RWTH Aachen University. Right-hand dominance of the participants was established by means of the Edinburgh handedness inventory (Oldfield, 1971).

### Affective stimuli

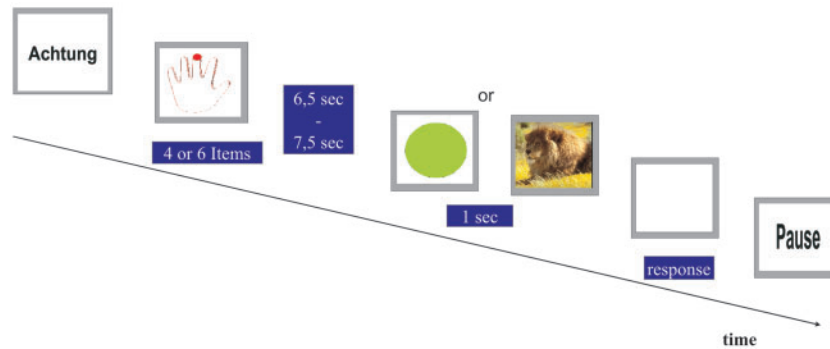
The stimuli used in this study consisted of 72 emotionally charged or neutral pictures selected from the IAPS (Lang *et al.*, 1999). We chose 24 negative, 24 neutral and 24 positive pictures from 3 categories: faces, person and animals with a balanced amount of pictures (i.e. 8) per category. Pictures were selected based on normative valence and arousal ratings from the IAPS technical manual. The mean arousal rating of the selected pictures was 5.3 for negative, 4.8 for positive and 3.6 for neutral pictures (scale ranging from 0 to 9; 0 = low arousal, 9 = high arousal). The mean valence rating of the selected pictures was 3.3 for negative, 7.2 for positive and 5.2 for neutral pictures (scale ranging from 0 to 9; 0 = negative valence, 9 = positive valence).

Although all stimuli had been rated in a normative sample, we assessed the affective response of our subjects in an explicit rating. After the functional magnetic resonance imaging (fMRI)—experiment, each subject rated the valence and arousal of all employed pictures in a fashion comparable to the approach used to calibrate the IAPS. These ratings were evaluated and compared with the normative data of the IAPS stimuli.

In our study we aimed at investigating, whether emotionally charged stimuli are processed differently under different loads of concurrent cognitive demand. Crucially, while the stimuli have to be overtly attended as they represent the (task-relevant) go-cue, their content is not relevant for performing the paradigm. This allows us to look for the modulation of bottom-up driven stimulus processing and ultimately the modulation of this processing by concurrent cognitive demand. An explicit rating of the pictures or the evoked emotional state during the fMRI session; however, would have directed attention towards the emotionality of the pictures and/or the subjects own emotions, introducing a potential confound. In other words, only by not having subjects rate the pictures on-line, we could address the question whether the automated processing of their (emotional) content is modulated by the experimental manipulation of cognitive load.

### Experimental procedure

The basic setup of all experimental trials was as follows: each event started with a cue ('Achtung'—Attention) indicating the next trial. Each trial began with the presentation of a schematised left or right hand for 1 s. Subsequently, the sequence that had to be memorized by the subjects was indicated by visual cues (red dots on the fingers) presented for 250 ms each. The indicated sequences consisted of either



**Fig. 1** Time line of the experimental trials. Each trial began with the presentation of a schematized left or right hand for 1 s. Subsequently, visual cues (red dots on the fingers) indicating either a four (easy condition) or a six (difficult condition) item, i.e. fingers, was presented for 250 ms each. Following the demonstration of the sequence, a blank screen was presented for a uniformly jittered delay lasting between 6.5 and 7.5 s. After that one of the 72 emotional pictures from the IAPS or a control stimulus (green dot) was presented for 1 s. The subjects' task was to reproduce the sequence they had been shown as fast and correctly as possible by button presses. Following the response there was a variable (7–11 s) inter-trial interval during which a blank screen was shown.

4 (easy condition) or 6 (difficult condition) items, i.e. fingers. Following the demonstration of the sequence, a blank screen was presented for a uniformly jittered delay lasting between 6.5 and 7.5 s. Finally, either one of the 72 emotional pictures from the IAPS (Lang *et al.*, 1999) or a control stimulus (green dot) was presented for 1 s (Figure 1). The subjects were instructed to reproduce the memorized sequence as fast and correctly as possible after the picture or dot had disappeared by pressing buttons on an magnetic resonance imaging (MRI)-compatible response pad (LumiTouch, Burnaby, Canada). That is, the IAPS pictures (or circle in the control condition) served as go-cue for the reproduction-part of the memory task. Following the response there was a variable inter-trial interval between 7 and 11 s (uniformly jittered, mean 9 s) during which a blank screen was shown again.

All visual stimuli were presented using the software presentation (Neurobehavioral Labs, Version 12.0) and on a custom-built, shielded thin-film transistor (TFT) screen at the rear end of the scanner visible via a mirror mounted on the headcoil ( $14^\circ \times 8^\circ$  viewing angle, 245 mm distance from the subject's eyes).

The experiment consisted of 16 distinct event-types (left and right hand; sequence-lengths of 4 or 6 items; neutral, positive, negative pictures or green dot), each of which was presented six times. That is, each of the eight conditions in our  $2 \times 4$  factorial design (e.g. short sequence-negative picture) was present in 12 trials, half of which were executed with the right, half with the left hand. The event order and the relationship between response hand, sequence-length and pictures were pseudo-randomized and counter-balanced across subjects.

### Behavioural data analysis

The behavioural measurements taken during the fMRI experiment were analysed off-line using MATLAB (MathWorks, Natick, MA, USA). The effect of the experimental factors of sequence lengths, go-cue (three types of

pictures/dot, cf. above) on mean reaction-time and percentage of correct responses were compared by repeated measurement analyses of variance (rmANOVA). If the effect of a factor was significant, pairwise comparison were performed by T-tests ( $P < 0.05$ , corrected for multiple comparisons using Tukey's procedure).

### fMRI

Images were acquired on a Siemens Trio 3T whole-body scanner (Erlangen, Germany) at the Research Center Jülich, Germany, using blood-oxygen-level-dependent (BOLD) contrast [gradient-echo echo planer imaging (EPI) pulse sequence, repetition time (TR) = 2.2 s, in plane resolution =  $3.1 \times 3.1$  mm, 36 axial slices (3.1 mm thickness)] covering the entire brain. Image acquisition was preceded by 4 dummy images allowing for magnetic field saturation. These were discarded prior to further processing. Images were analysed using statistical parametric mapping (SPM5) ([www.fil.ion.ucl.ac.uk/spm](http://www.fil.ion.ucl.ac.uk/spm)). First, the EPI images were corrected for head movement by affine registration using a two-pass procedure, by which images were initially realigned to the first image and subsequently to the mean of the realigned images. After realignment, the mean EPI image for each subject was spatially normalized to the Montreal Neurological Institute (MNI) single subject template using the 'unified segmentation' approach (Ashburner and Friston, 2005). The resulting parameters of a discrete cosine transform, which define the deformation field necessary to transfer the subjects data into the regional probability maps of the MNI space were then combined with the deformation field transforming between the latter and the MNI single subject template. Subsequently, the deformation was applied to the individual EPI volumes that were hereby transformed into the MNI single subject space and resampled at  $2 \times 2 \times 2$  mm<sup>3</sup> voxel size. The normalized images were spatially smoothed using an 8 mm full-width half-maximum (FWHM) Gaussian kernel to meet the statistical

requirements of the General Linear Model and to compensate for residual macroanatomical variations across subjects.

### Statistical analysis

The fMRI data were analysed using a general linear model as implemented in SPM5. Each retrieval cue condition (negative, positive, neutral pictures and dot) as well as encoding and retrieval was separately modelled for sequence-lengths of four and six items. The encoding condition comprised the time during the visual presentation of the red dots indicating the sequence to be remembered, while the retrieval condition captured the manual response of the subjects, i.e. the reproduction of the remembered sequence. Boxcar reference vectors of the respective conditions' timings and durations were convolved with a canonical haemodynamic response function and its first-order temporal derivative. Low-frequency signal drifts were filtered using a cut off period of 128 s. Parameter estimates were subsequently calculated for each voxel using weighted least squares to provide maximum likelihood estimators based on the temporal autocorrelation of the data (Kiebel and Holmes, 2003). No global scaling was applied. For each subject, simple main effects for each of the experimental conditions as outlined above were computed by applying appropriate baseline contrasts. These individual first-level contrasts were then fed into a second-level group-analysis using an ANOVA (factor: condition, blocking factor subject) employing a random-effects model. Modelling the variance components, we allowed for violations of sphericity by assuming non-independence across images from the same subject and allowing unequal variances between conditions and subjects using the standard implementation in SPM 5. Simple main effects of each task (*vs* the resting baseline) as well as comparisons between experimental factors were tested by applying appropriate linear contrasts to the ANOVA parameter estimates. The resulting SPM (T) maps were then thresholded at  $P < 0.05$ , unless otherwise mentioned, corrected for multiple comparisons according to the theory of Gaussian random fields (Worsley *et al.*, 1996). Activations were anatomically localized using version 1.5 of the SPM anatomy toolbox ([http://www.fz-juelich.de/inm/spm\\_anatomy\\_toolbox](http://www.fz-juelich.de/inm/spm_anatomy_toolbox), Eickhoff *et al.*, 2005).

## RESULTS

### Behavioural data

The explicit rating of the employed pictures by our subjects yielded the following results: Negative pictures: Mean arousal  $4.83 \pm 1.50$  (IAPS:  $5.30 \pm 1.10$ ,  $P > 0.05$ ). Mean valence  $3.11 \pm 1.08$  (IAPS:  $3.33 \pm 0.88$ ,  $P = 0.077$ ). Neutral pictures: Mean arousal  $2.95 \pm 0.94$  (IAPS:  $3.60 \pm 0.84$ ,  $P < 0.01$ ). Mean valence  $5.43 \pm 0.69$  (IAPS:  $5.21 \pm 0.44$ ,  $P = 0.077$ ). Positive pictures: Mean arousal  $5.01 \pm 0.97$  (IAPS:  $4.84 \pm 0.82$ ,  $P = 0.438$ ). Mean valence  $7.38 \pm 0.65$  (IAPS:  $7.25 \pm 0.62$ ,  $P = 0.257$ ).

**Table 1** Mean and s.e. of the error rate of positive, neutral and negative pictures relative to the control condition (green dot)

Items	Mean/s.e. (difference to the control condition)		
	Positive	Neutral	Negative
4	$4.4 \pm 1.5$	$5.5 \pm 2.2$	$2.3 \pm 1.6$
6	$-2.5 \pm 2.7$	$0 \pm 2.8$	$5.5 \pm 2.7$

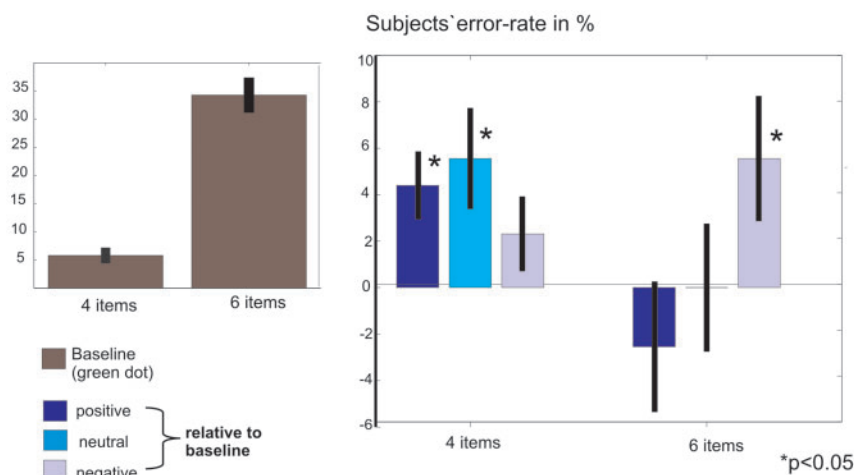
Analysis of the behavioural data recorded in the scanner revealed significantly higher error rates at sequence-lengths of six items (mean:  $34.3 \pm 3.1$ ) than at sequence-lengths of four items (mean:  $5.8 \pm 1.4$ ). More detailed information about emotional pictures' mean- data and s.e. can be found in Table 1. All pictures except the negative ones enhanced the error rate significantly when sequence-length was four items (all pictures *vs* control  $P < 0.003$ ; positive *vs* control  $P < 0.005$ , neutral *vs* control  $P < 0.015$ , negative *vs* control  $P < 0.160$ ). There was, however, a differential effect of the stimulus content on retrieval of the longer sequences: negative pictures led to a higher error-rate ( $P < 0.047$ ), positive pictures to a lower ( $P < 0.372$ ) and neutral pictures showed a non-significantly different error rate ( $P < 1.00$ ) relative to the control condition, i.e. circle (Figure 2). The difference in error rates evoked by positive and negative pictures was also significant ( $P < 0.020$ ).

We thus found a main effect of sequence length on error rate, as the longer sequence resulted in significantly more errors, indicating higher cognitive demand. Secondly we found a picture context by sequence length interaction. Although there was a significant main effect of 'picture' at shorter sequences, there was a differential influence of emotional content on error rates in the more difficult condition. Finally, we failed to find any significant gender differences in any analysis.

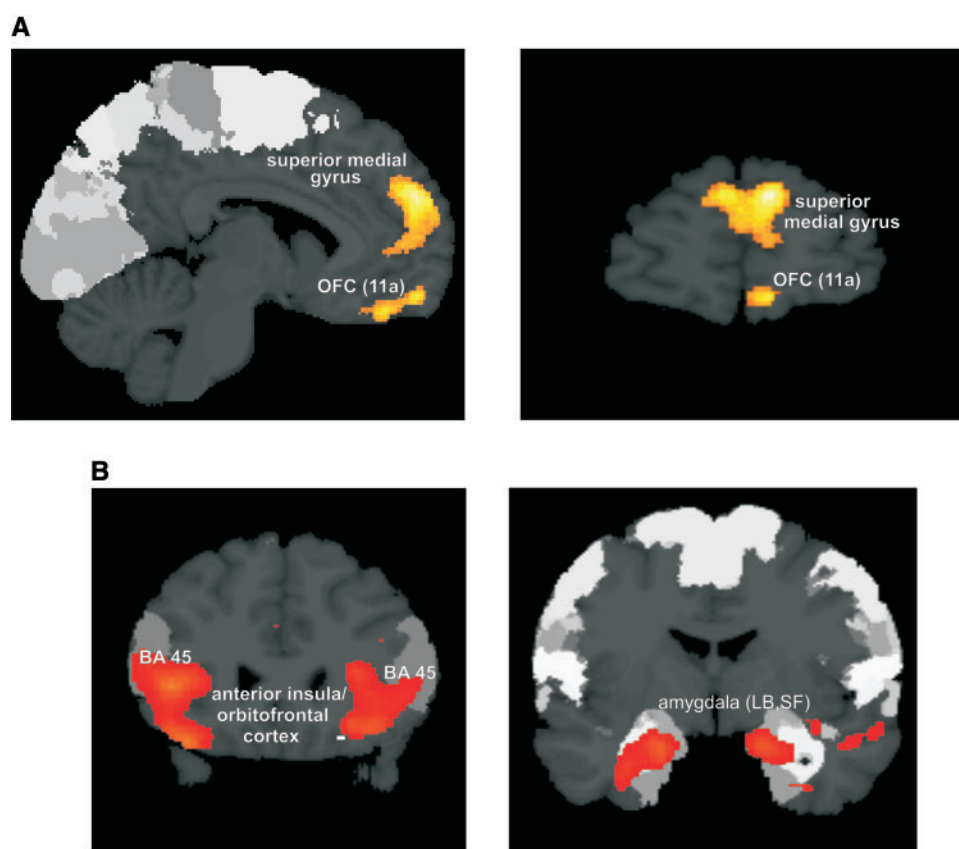
### Imaging data

Areas involved in the processing of emotional stimuli were identified by contrasting pictures rated by the subjects as positive or negative with (i) those rated as neutral and (ii) the low level control condition (green circle). To delineate the network involved in the cognitive (motor memory) task we performed a conjunction analysis over the fMRI activations associated with all encoding and retrieval conditions (these findings are shown in the Supplementary Data). In order to address the interaction between emotion and cognition, we then tested for areas showing decreased activation during emotional cues when longer sequences had to be memorized (in conjunction with the respective low-level resting baseline contrast) and also assessed the reverse contrast (areas showing higher activation during the emotional cues following the memorization of longer sequences).





**Fig. 2** Behavioural data as obtained in the scanning session. All pictures from IAPS increased the error-rate relative to the resting control condition at reproducing the shorter sequences (four items). For the influence on the reproduction of the more difficult sequences (six items), we observed differential valence effects: negative pictures increased the error-rate relative to the control condition, positive ones decreased the error-rate and neutral ones had an identical error-rate compared with the control condition.



**Fig. 3** Imaging- data for network of the processing of emotional stimuli. Relative to neutral pictures there is increased activation in OFC and dorsal medial prefrontal cortex to emotional (positive/negative) stimuli. (A) Relative to the control condition there is also increased activation of amygdala, BA45 and anterior insula/OFC (B) shown here as a differential contrast across positive and negative pictures at sequence-lengths of four and six items and neutral pictures or rather control condition.

### Imaging data—processing of emotional stimuli

Relative to neutral images, emotional (positive and negative) pictures evoked significantly stronger activation (Figure 3a) in the dorsal medial prefrontal cortex (superior medial

gyrus;  $-9/56/24$ ) and the left medial orbitofrontal cortex (OFC) ( $-6/57/-18$ ). Moreover, we found significantly higher activation by emotional as compared with neutral pictures bilaterally in the lateral OFC ( $-46/25/-2$  and

**Table 2** Increased activation at emotional pictures relative to the control condition (green dot)

Location	Hemisphere	Histological assignment	Local maximum
Medial OFC	left		−6/54/−14
Amygdala	left	LB/SF	−19/−4/−25
	right	LB/SF	18/−3/−23
Lateral OFC	left		−32/33/−18
	right		39/35/−12
Insula/frontal operculum	left		−53/25/2
	right		30/25/7
Inferior frontal cortex	right	BA 45	39/22/24
Visual cortex	left	hOC3v	24/−77/−12
	right	hOC3v	30/−77/−12
Fusiform gyrus	left		41/−51/−21
	right		−39/−50/−22
Lingual gyrus	left		−20/−47/−9
	right		18/−50/−2

Amygdala: Amunts *et al.* (2005); BA45: Amunts *et al.* (1999); hOC3v: Rottschy *et al.* (2007).

Note that only the three most significant locations for the extended visual cortex activation are reported on each hemisphere. In addition, for the visual cortex histological assignment was based only on local maxima as opposed to the volume-based assignments employed in the other tables.

32/27/−11) and BA 45 (−50/29/6 and 56/30/3) as well as in the right middle temporal gyrus (hOC5; 50/−72/−2) and right temporal pole (47/8/−27).

In comparison to the low-level control condition (circle) emotional stimuli also caused significantly stronger activation bilaterally in the amygdala, anterior insula/frontal operculum, lateral OFC (Figure 3b) and medial prefrontal cortex (Table 2). Additional differences were seen in the right inferior frontal cortex. As expected, extended regions of stronger activation were also found in the visual cortex, in particular in the ventral stream including the occipitotemporal cortex.

No brain region was significantly stronger activated by positive as compared with negative pictures and *vice versa*. We did not find significant differences in amygdala activity depending on the emotional valence of the stimuli.

### Imaging data—modulating the processing of emotional stimuli by cognitive demand

In order to investigate the interaction between cognitive load and the processing of emotional stimuli, we contrasted the activity associated with the emotional cue periods following the memorization of short relative to long sequences. When testing for increased activity in the (emotional) cue period following the memorization of six-item sequences relative to that following the four-item sequences, activation of a widespread network was observed. In particular, we found significantly higher activity closely mirroring the motor-memory network described above with additional activation

in the bilateral dorsolateral prefrontal cortex (DLPFC) (Figure 4a and Table 3).

While these results primarily indicate a higher engagement of frontoparietal action-related regions by the more demanding task, the key comparison for investigating influences on the processing of emotional stimuli was the reversed contrast. Here we tested where in the brain the activity was reduced in response to the emotional cues under the condition of concurrent higher cognitive load, i.e. the performance of the more difficult memory task. To furthermore exclude regions that only reflected attenuated processing of pictures *per se*, this comparison was performed by testing for an interaction between stimulus content and cognitive load (emotional pictures during easy task > emotional pictures during difficult task) > (neutral pictures during easy task > neutral pictures during difficult task). This interaction revealed significant attenuation specifically of emotional pictures only in the medial OFC (−5/39/−23) and the bilateral amygdala (LB; −18/−2/−26 and SF; 26/−3/−17) (Figure 4b). Results were significant at  $P < 0.05$  on the cluster-level level (cluster forming threshold of voxel-level  $P < 0.0001$ ).

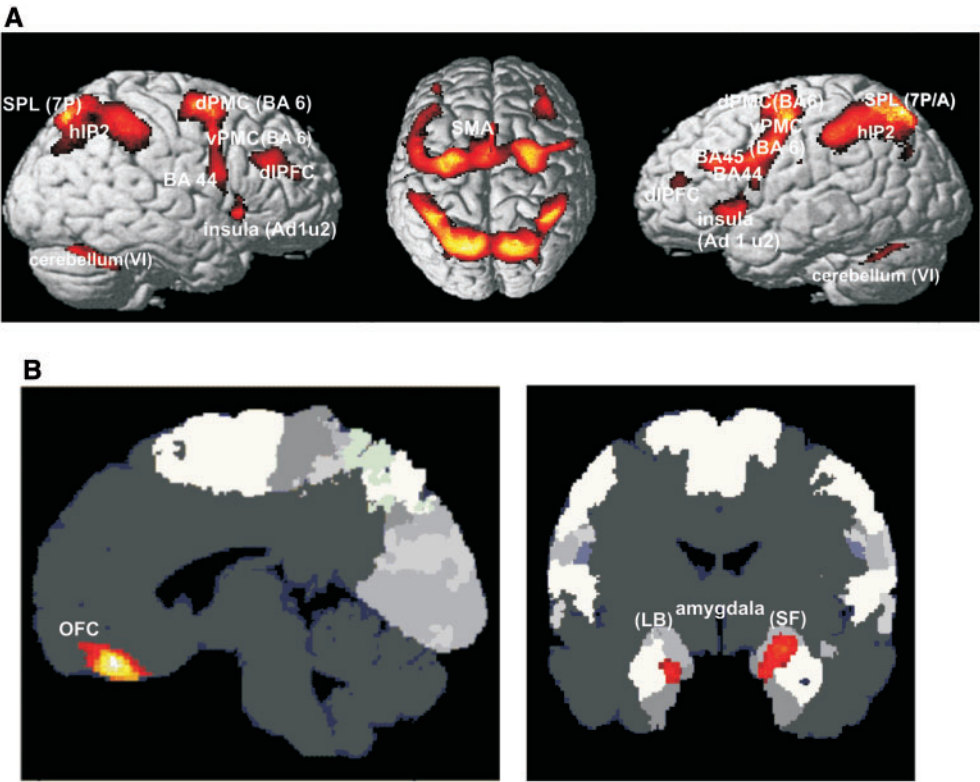
To test for neuronal activation associated with the observed behavioural effects, we correlated the difference in activation evoked by negative and positive pictures, respectively relative to the control condition (green circle) and the corresponding changes in error rates. No significant activation was found at the corrected level. At a more liberal threshold; however, we observed a correlation between the increase in error rates and increased activation in the medial prefrontal cortex (mPFC) (23/42/20). On the other hand, increased activation in right OFC (33/56/1), left BA 45 (−53/17/33) and left insula (lg1; −33/−30/4) (Kurth *et al.*, 2010) correlated with better performance elicited by positive picture, albeit again on the uncorrected level.

## DISCUSSION

The aim of this study was to investigate whether responses to emotional stimuli become attenuated when concurrent cognitive demand is increased, even when these stimuli are task-relevant and have to be overtly attended to in order to obtain the go-cue. Expectedly, activity evoked by the emotional stimuli was found in areas known to be involved in these processes such as the amygdala, the insula, the orbitofrontal and dorsomedial prefrontal cortices (dmPFCs). The key finding of this study is that processing of task-relevant and hence attended emotional stimuli was influenced by concurrently cognitive demand. Under the concurrent performance of the more difficult task, activity in central areas of emotion-processing, in particular amygdala and OFC, was significantly reduced.

### Processing of emotional stimuli

Electrophysiological recordings and neuroimaging have supported key positions of the amygdala, OFC, dmPFC,



**Fig. 4** Imaging- data for modulating the emotional processing by cognitive demand. **(A)** In comparison to the easy task (Emo4: positive and negative pictures at sequence-lengths of four items) the more difficult task (Emo6: positive and negative pictures at sequence-lengths of six items) evoked stronger activation in the superior parietal lobe and the premotor cortex, known to be involved in motor planning and attention. A detailed description of the clusters (referenced according to the labels in this figure), including local maxima coordinates and cytoarchitectonic substrates, is given in Table 3. **(B)** The suppression of the processing of emotional stimuli is identified by an interaction between stimulus content and cognitive load (emotional pictures during easy task > emotional pictures during difficult task) > (neutral pictures during easy task > neutral pictures during difficult task). At concurrently execution of the difficult task, amygdala and OFC are activated significantly less by emotional stimuli **(B)**.

**Table 3** Increased activation in the emotional cue period following a 6-item sequence relative to that following a 4-item sequence

Location	Hemisphere	Histological assignment	Local maximum
SPL	left	7A/7P	−10/−69/57
	right	7A/7P	16/−69/54
IPS/IPC	left	hIP1–hIP3, BA 2	−38/−44/44
			−38/−53/54
vPMC	right	hIP1–hIP3, BA 2	40/−44/50
	left	BA 6/BA 44/BA 45	−40/2/33
			−50/0/42
	right	BA 6/BA 44	48/6/22
dPMC	left	BA 6	−27/−4/54
	right	BA 6	29/2/60
SMA	left	BA 6	−4/0/63
MCC	left		−8/14/44
DLPFC	left		−36/50/14
	right		35/47/21
Insula	left		−36/21/−2
	right		35/47/21
Cerebellum	left	Lobulus VI/Crus I	−33/−57/−35
	right	Lobulus VI/Crus I	37/−53/−34
Basal ganglia	left	Ncl. Pallidus	−16/−1/−6

7A, 7P, hIP3: Scheperjans *et al.* (2008); Pft: Caspers *et al.* (2006); hIP1, hIP2: Choi *et al.* (2006); BA6: Geyer (2003); BA44: Amunts *et al.* (1999); VI/Crus I: Diedrichsen *et al.* (2009); Amygdala: Amunts *et al.* (2005).

cingulate gyrus and insula in response to emotional stimuli (Canli *et al.*, 1998; Phan *et al.*, 2005; Urry *et al.*, 2006). In line with this view, we also observed robust activation of these regions by our emotional stimuli. Importantly, however, there is good evidence, that these regions sustain different aspects of processing and evaluation of emotional material.

To differentiate processing of emotional content from the appraisal of complex stimuli like the IAPS pictures *per se*, we implemented a low level control condition (green dot) and a neutral picture from the IAPS as high level control condition.

The comparison of emotional pictures (negative as well as positive) against the green dot (low level control condition) reveals regions that are involved in the processing of emotional pictures, while the comparison against the neutral pictures only indicates areas that are specifically involved in processing emotionally charged material. This allowed to further differentiate the roles of the different brain regions engaged in processing emotional stimuli.

The OFC appears to play a critical role in the representation of reward value and its guidance of goal-directed behaviour (Rolls, 1999). Other studies have implicated the OFC in the production of affective states, as e.g. increased

activation of the OFC has been demonstrated during the perception of pleasant and unpleasant odours and tactile stimuli (Francis *et al.*, 1999). Kiebel *et al.* (2008) proposed a cortical anatomic-temporal hierarchy, in which the OFC represents temporally stable states such as personal beliefs and preferences. According to this model, the OFC should thus code individual values and conceptions as well as playing an important role in explicit appraisal, i.e. the conscious formation of an opinion. We would hence argue, that the observed OFC activation reflects an appraisal of the pictures based on values and experience. This interpretation is well in line with our observation, that the OFC was specifically engaged by emotional as compared with neutral stimuli, as these should elicit stronger resonance with the preferences and values coded in the OFC.

Similarly, the medial prefrontal cortex was also stronger activated by emotional than neutral stimuli. This region is widely regarded as an integrative region, linking the emotional signals provided, e.g. by the amygdala, to the current cognitive and social context (Frith and Frith, 2003; Saxe and Kanwisher, 2003). One specific aspect in this process is the combination of cognitive and emotional states with self-referential processes and information about one's own self (Mitchell *et al.*, 2005). That is, emotional signals were judged by subjects' own experience and socio-emotional consequences of one's own actions and the mental state of others (Aichhorn *et al.*, 2006). Consequently, studies with brain-lesion patients have also demonstrated that the medial prefrontal cortex plays an important role for subjective control of behaviour, potentially due to problems in integrating social, emotional, cognitive and self-reflexive aspects (Eslinger and Damasio, 1985; Hornak *et al.*, 2003; Shamay-Tsoory *et al.*, 2004). The observed activation may thus reflect the self-reflexive appraisal of their emotional valence. This interpretation of a more specific appraisal of emotionality, rather than an automated processing of a picture *per se*, again fits well with the relative stronger activation to emotional than neutral pictures.

The insula and amygdala, in contrast, are considered as implicit processing systems (Shah *et al.*, 2009) involved in the automatic identification of emotional information (Adolphs *et al.*, 2002; Phillips *et al.*, 2003a, b). Along the same line, they have been implicated in the subconscious detection of emotional salience (Anderson and Phelps, 2001) and attentional reorientation to this. That is, the amygdala seems mainly involved in the regulation of arousal based implicit stimulus-driven processing of emotional material. The insula has primarily been associated with processing of disgust (Phillips *et al.*, 2004). Nevertheless this brain structure has a broader role in emotion processing (Phan *et al.*, 2002), e.g. during the processing of emotionally salient pictures (Simmons *et al.*, 2004) or the emotional modulation of verbal prosody (Ethofer *et al.*, 2009). Additionally, the insula has also been shown to be instrumental in the detection, interpretation and regulation of internal bodily states

(Critchley, 2003; Critchley *et al.*, 2005). It may hence be argued, that the observed insular activations reflect an implicit processing and appraisal of the emotional content in the displayed stimuli, whose output; however, is less related to attentional saliency but rather autonomic responses. As both regions (amygdala and insula) were only significantly activated in comparison to the control stimulus but not the neutral pictures, we would furthermore conclude, that neutral pictures may have been processed in a similar fashion. This may suggest, that subconscious monitoring of (emotional) salience may work in a highly automated manner triggered by the presentation of a complex stimulus like the IAPS pictures.

### **Modulating the processing of emotional stimuli by cognitive demand**

In our study the interaction of emotion and cognition demonstrated that under the concurrent engagement in a more demanding cognitive (motor short-term memory) task, the activation evoked by attended but not task-relevant emotional stimuli in the OFC and the amygdala (LB/SF) was significantly reduced. Importantly, the significant stimulus  $\times$  cognitive load interaction clearly demonstrated that these effects in the OFC and bilateral amygdala are attributable to the reduced processing of emotional material and not of attenuated picture processing *per se*. Based on this observation and the discussion above, it thus seems that the implicit processing of salient stimuli (amygdala) and the value-based appraisal (OFC) of emotionally charged stimuli becomes attenuated in the presence of a more demanding cognitive task.

A possible explanation why these two key areas of the emotional network are suppressed during the more demanding task may be that cognitive processing draws attentional resources away from them. This could be implemented by top-down modulated inhibition of these regions (potentially by the lateral prefrontal cortex), rendering them less sensitive to incoming stimuli (Drevets and Raichle, 1998). On the other hand, emotional and non-emotional information may compete for (limited) attentional resources (Erthal *et al.*, 2005). In this case, task-irrelevant emotional stimuli may be outside the spotlight of attention and hence processing would be attenuated without the need for explicit inhibition. Supporting evidence for attention-based view comes from tasks where non-emotional stimuli visually compete with emotional pictures for attention (Pessoa *et al.*, 2002b; Okon-Singer *et al.*, 2007). Moreover, emotional circuits could be down-regulated by re-focussing attention even after emotional circuits have been engaged, indicating that regions, such as the OFC and the amygdala, operate flexibly and can be modulated by current contextual demands (Van Dillen and Koole, 2007).

One of the crucial implications from our experiment is that apparently such down-regulation of the processing of emotional stimuli due to active inhibition or to re-allocation



of attention may be found even when emotional stimuli are task-relevant and thus cannot be ignored. It is important to emphasize, that the pictures themselves were task-relevant insofar as subjects had to attend overtly to these in order to get the go-cue for the sequence reproduction. It should be mentioned; however, that the emotional content *per se* was not task-relevant. Consequently, subjects must have visually processed these stimuli and registered their content. Nevertheless, the concurrent presence of higher demands on memory and motor preparation seems to attenuate the responses to these in the amygdala and the OFC, indicating that sensory perception of an affectively valenced stimulus and the evocation of the processing of emotional stimuli may be dissociable from each other. In other words, the cognitive engagement did not cause subjects to miss the stimuli, but rather it dampened the responsiveness of the affective network to them.

While reduced amygdala activation to emotional stimuli under increased cognitive demand has been reported in earlier studies (Blair *et al.*, 2007; Erk *et al.*, 2007) neither of these groups observed a modulation of the OFC as found here. This difference may relate to the experimental setup, as both earlier studies investigated the response to task-irrelevant emotional distracters. As detailed above, however, it seems that the OFC is particularly involved in the appraisal of emotional valence. Hence, it may be speculated that in these previous experiments, participants may have ignored the emotional distracters already in the easy condition so that consequently no OFC activation could be attenuated by the more demanding task. Evidently, our subjects could not ignore the stimuli representing the go-signal for sequence reproduction leading to the discussed dissociation between perception and emotional appraisal when the more difficult task was performed. On the other hand, sample differences and consideration of experimental power may also have contributed as e.g. Erk *et al.* (2007) only examined 12 female subjects, whereas our sample comprised 36 subjects with balanced gender proportions.

In summary, we would thus propose, that the affective response to emotionally charged and physically perceived stimuli may be attenuated by concurrent cognitive processing, reflecting a relocation of resources, potentially mediated by top-down influences of regions such as the DLPFC and the supplementary motor area (SMA).

### Modulation of cognition by emotional stimuli

As evident from our behavioural data, emotional stimuli also influence task performance. In particular, all pictures (emotional and neutral pictures) increased the error rate relative to the control condition in the easier task. This effect may relate to the higher saliency of the images (compared with the circles serving as the control condition) and hence their higher potential for distraction (Fenske and Raymond, 2006).

For the more difficult condition we found a differential effect of picture valence. Although negative pictures increased the error rate, positive pictures actually enhanced performance. Similar results were found by Bartolic *et al.* (1999) as well as Gray (2001), who examined the effect of positive and negative emotion on cognitive processing and reported significantly improved verbal working memory performance in the presence of positive affect and significant deterioration in the presence of a negative one. It has been argued that the decline in performance may be due to increased information processing load and the drain of attentional resources by the emotional stimuli that otherwise might be devoted to task performance (Muller *et al.*, 2008). This view, however, seems to hold mainly for negative emotions as evident from the studies cited above, our own data and previous work outlining how emotions impair or enhance attention (Bargh *et al.*, 1996; Anderson and Phelps, 2001; Anderson, 2005; Habel *et al.*, 2007; Koch *et al.*, 2007). It may be assumed that the decline in performance brought upon by negative pictures could be attributed to their attentional salience and greater evolutionary significance, which, as discussed above, might be signalled by the amygdala. However, as we did not observe significantly higher amygdala activation for negative relative to positive pictures but in fact a stronger response of the premotor cortex, a definite conclusion about the neurobiological underpinnings of the hypothesized automatic attentional capture remains elusive.

In contrast, higher success rate for positively valenced pictures may relate to increased levels of forebrain dopamine associated with these. That is, a dopamine release, presumably in the ventral striatum, triggered by the respective stimuli would not only result in positive affect but also enhancement of cognitive capacities (Ashby *et al.*, 1999). This would be in line with the results of behavioural studies showing that positive affect enhances a broad range of cognitive processing (Ashby *et al.*, 1999).

### CONCLUSION AND OUTLOOK

Here we have shown that engagement in a more difficult and hence cognitively demanding task reduces responses to affective stimuli in two areas central to the processing of emotional stimuli, the amygdala and the OFC. As stimuli were task-relevant and hence had to be processed perceptually, we would interpret this as a specific attenuation of affective responses by concurrent cognitive processing, reflecting a relocation of resources that may be mediated by top-down influences. A better knowledge of these mechanisms underlying the modulated processing of emotional stimuli by cognitive demand may lead to a better understanding of the neurobiology of therapeutic skills, as applied, e.g. as part of cognitive behaviour therapy approaches in borderline personality disorder.

### SUPPLEMENTARY DATA

Supplementary data are available at SCAN online.

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